The burden of bacterial antimicrobial resistance in the WHO Eastern Mediterranean Region 1990–2021: a cross-country systematic analysis with forecasts to 2050

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Summary

Background Antimicrobial resistance (AMR) is an urgent global crisis and one of the world's most complex challenges. Although there is increasing evidence of its impact on human mortality and morbidity, precise burden estimation has many challenges, and thus far has been elusive for the Eastern Mediterranean Region. Here, we present a comprehensive time-trend analysis of regional and country-level AMR burden estimates in the WHO Eastern Mediterranean Region (EMR), between 1990 and 2021, with forecasts up to 2050.

Methods We estimated deaths and disability-adjusted life-years (DALYs) attributable to and associated with AMR for 11 infectious syndromes, 22 bacterial pathogens, and 84 pathogen–drug combinations for the WHO EMR and each of its countries from 1990 to 2021. Data were obtained from mortality registries, surveillance systems, hospital records, systematic literature reviews, and other sources. We based our modelling approach on five broad components: the number of deaths in which infection had a role, the proportion of infectious deaths attributable to a given infectious syndrome, the proportion of infectious syndrome deaths attributable to a given pathogen, the percentage of a given pathogen resistant to an antimicrobial drug of interest, and the excess risk of mortality (or duration of an infection) associated with this resistance. These components were then used to estimate the disease burden by using two counterfactual scenarios: deaths and DALYs attributable to AMR (considering an alternative scenario where drug-resistant infections are replaced with susceptible infections), and deaths and DALYs associated with AMR (considering an alternative scenario where infections would not occur at all). Predictive statistical modelling was applied to generate estimates of AMR burden for each country. We also generated AMR burden forecasts up to 2050. We generated 95% uncertainty intervals (UIs) for the final estimates by taking the 2·5th and 97·5th percentiles across 500 draws through the multistage computational pipeline, and models were cross-validated for out-of-sample predictive validity.

Findings We estimated 380 000 deaths (95% UI 332 000–426 000) associated with bacterial AMR and 92 800 deaths (78 300–111 000) attributable to bacterial AMR in the EMR in 2021. In the past 31 years, there was considerable variation in AMR mortality trends across countries of the region and different age groups. Between 1990 and 2021, associated deaths among children younger than 5 years decreased by 50·0% (38·2–62·0), while those among adults aged 70 and older rose by over 85·7% (95% UI 57·0–115·7). Six pathogens were identified as the primary generators of burden: *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus aureus*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*. A substantial increase in the AMR burden due to *S aureus* was observed between 1990 (28 200 deaths [21 600–34 000]) and 2021 (49 500 deaths [43 100–56 200]); consequently, in 2021, methicillin-resistant *S aureus* was a leading pathogen–drug combination for most countries in the region for deaths and DALYs attributable to, and associated with AMR. Somalia had the highest age-standardised mortality rates in the region: for deaths attributable to and associated with AMR per 100 000 population in both 1990 and 2021; conversely, the country with the lowest burden in the EMR was Qatar. By 2050, the number of deaths attributable to AMR in region is forecasted to reach 187 000 (157 000–223 000) and deaths associated with AMR were projected to reach 752 000 (629 000–879 000).

Interpretation Our study shows that bacterial AMR has been a serious public health threat in the EMR for more than 30 years, with a substantial fatal and non-fatal burden for priority bacterial pathogens and pathogen–drug combinations. The magnitude of this issue, future projects, and the inadequate response capacity in many countries underscore the need for more stringent regional leadership in this field. The insights gained from this study can direct targeted mitigation strategies for individual countries within the region, aiding in resource allocation and funding decisions, and emphasising the need for collaborative multisectoral endeavours among nations to address this issue.

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Research in context

Evidence before this study

Antimicrobial resistance (AMR) is recognised as one of the most important global hazards to public health and security. It is also a leading cause of mortality and disability around the world, especially in low-resource settings, as demonstrated by the 2021 global burden of AMR study. We searched PubMed for articles published between Jan 1, 2010, and Dec 31, 2024, analysing the prevalence and exposure to resistant bacteria in the WHO Eastern Mediterranean Region (EMR) using the search terms: "antimicrobial resistance AND Eastern Mediterranean Region", "drug-resistant infections AND WHO EMRO", "AMR burden AND Middle East", "antimicrobial resistance trends AND EMRO", and "AMR surveillance AND EMR countries". A 2022 publication identified increasing AMR prevalence trends in this region between 2017 and 2019; however, specific reports reporting on time trends of the burden of AMR (and methodologically rigorous projections) for member states or the region as a whole are scarce. Considering that AMR research and mitigation in EMR rely heavily on policy prioritisation and funding availability, there is an urgent need for a comprehensive, methodologically robust, and timely assessment of the regional and country-specific AMR burden, including both historical trends and forward-looking projections.

Added value of this study

To our knowledge, this is the most detailed and inclusive analysis of the burden of AMR in EMR to date, providing estimates for 22 countries, 11 infectious syndromes, 22 bacterial pathogens, and 84 pathogen–drug combinations for the period between 1990 and 2021, and forecasts up to 2050. We used major methodological innovations from the 2021 global burden of AMR study and employed two different counterfactual scenarios to estimate the magnitude of the problem throughout the EMR where the burden has, thus far, been largely undefined. In terms of scale, this study substantially advances previous attempts to estimate the burden of AMR in this region, particularly considering the number of data sources, countries, and pathogen–drug combinations included in this analysis. Additionally, this study enables relevant comparisons of other causes of death by building on estimates of disease incidence, prevalence, and mortality from the Global Burden of Diseases, Injuries, and Risk Factors Study 2021.

Implications of all the available evidence

Our estimates offer an in-depth quantitative exploration of the burden of AMR in EMR for a 31-year period and offers stringent predictions, highlighting substantial differences between subregions and countries. This establishes a much-needed baseline for understanding the AMR burden across the region, enabling meaningful comparisons over time and across countries, while providing a foundation for assessing the impact of interventions. By estimating almost 400 000 deaths associated with bacterial AMR in 2021 (and showing that two-thirds of all bacterial deaths are already associated with resistance), the findings can be considered as pivotal for informing cost-effective public health investment decisions and inciting better implementation of national action plans against AMR. Additionally, by underscoring specific pathogens and bacteria–drug combinations that underpin the majority of the estimated burden, our findings might specifically inform targeted infection prevention and control programmes and antibiotic stewardship initiatives, and identify research needs for the development of novel diagnostic tests, antibacterials, and vaccines that will aid in alleviating the projected future burden.

Introduction

Antimicrobial resistance (AMR), often called the silent pandemic, is a major global threat to human health, with wide-ranging effects on animal welfare, food safety, the environment, and the economy. It is projected that AMR will cause up to 10 million deaths annually by 2050.[1] While these numbers were initially met with scepticism,[2,3] they were supported by the most recent global assessment of AMR burden, which estimated 1·14 million deaths attributable to and 4·71 million associated with bacterial AMR in 2021, projecting up to 8·22 million associated deaths annually by 2050.[4]

Different areas of the world present unique challenges in combating AMR. The WHO Eastern Mediterranean Region (EMR), where approximately 10% of the global population reside,[5] has a lower mean life expectancy than the global mean, with a 21-year gap between Kuwait and Somalia.[5] Harsh social and economic conditions, including wars and conflicts, disrupt demographics and strain health systems.[6] Due to competing public health needs and priorities, particularly in emergency settings, addressing AMR in the EMR has been frequently neglected. Regional reports from 2016 acknowledge the growing threat of AMR,[7] and demographic changes could additionally influence its burden.[4] In the past decade, AMR and antibiotic use data from EMR countries have increased,[8] with expedited efforts in the past decade.

The Strategic and Technical Advisory Group on AMR and the WHO Global Task Force coordinate key actions against AMR, with the EMR contributing regional perspectives.[9] Since the adoption of the Global Action Plan On Antimicrobial Resistance at the World Health Assembly in 2015,[10] most EMR countries have developed national action plans, reported antimicrobial consumption data to WHO's surveillance system, and introduced national infection prevention and control programmes in more than 70% of cases.[8] However, the absence of feasible, data-driven national AMR estimates has limited investment, hampered full implementation, and reduced private sector engagement.[1,2,4]

This study aimed to quantify bacterial AMR burden in the EMR, providing the first regional and country-level estimates (1990–2021) across diverse pathogens and pathogen–drug combinations using a robust methodology. We also aimed to provide detailed age-specific data and region-specific forecasts of the AMR burden through 2050. This manuscript was produced as part of the Global Burden of Disease (GBD) Collaborator Network and in accordance with the GBD Protocol.[11]

Methods

Overview and input data

This is the first in a collection of studies that aim to describe the regional burden of AMR in the EMR between 1990 and 2021, together with forecasts up to 2050. The study extends the results of the 2021 global burden of AMR study,[4] and uses its methodological approach.

Building on the 2021 global burden of AMR study,[4] this analysis offers granular, country-specific estimates for the EMR, aggregating all-age and age-specific deaths and disability-adjusted life-years (DALYs) from 1990–2021, with forecasts to 2050. DALYs were calculated as the sum of years of life lost due to premature mortality and years of healthy life lost due to disability. Disease burden associated with and attributable to AMR was estimated for 11 infectious syndromes, 22 bacterial pathogens, 16 drug categories (or combinations of drugs for which there is resistance) and 84 pathogen–drug combinations. In some analyses, countries belonging to the EMR were grouped by GBD regions (ie, eastern sub-Saharan Africa, north Africa and the Middle East, and south Asia) for comparability with other publications.

Global input data consisted of 520 million individual records or isolates covering 19 513 study-location-years, drawing on the GBD data framework and collaborator networks. From the GBD we leveraged multiple cause-of-death data, mortality surveillance data, linkage data, hospital discharge records, and outpatient and inpatient insurance claims (appendix 1 pp 13, 134). From our extensive collaborator network and other publicly available datasets we used microbiology data with and without patient outcomes, results of scientific studies, antibiotic resistance surveillance reports, pharmaceutical sales data, and antibiotic usage surveys. National action plan data were acquired from the global database for tracking antimicrobial resistance country self-assessment survey responses for the years 2018–2021 and the WHO AMR national action plan library. Full dataset details are in appendix 1 (pp 13) and described elsewhere.[4]

Modelling steps

Our modelling approach comprised five broad components: the number of deaths involving sepsis, the proportion of infectious deaths attributable to a given infectious syndrome, the proportion of infectious syndrome deaths attributable to a given pathogen, the percentage of a given pathogen resistant to an antimicrobial drug of interest, and the excess risk of death or duration of an infection associated with this resistance. This study followed GATHER guidelines[12] (appendix 1 pp 70, 107–108).

In the first modelling step, sepsis-related deaths were estimated using cause of death estimates from GBD 2021, defining sepsis as life-threatening organ dysfunction resulting from a dysregulated immune response to infection. Mixed-effects logistic regression models were applied to a dataset that included multiple cause-of-death records, hospital discharge records, Child Health and Mortality Prevention Surveillance (CHAMPs), and other surveillance data. This process predicted the proportion of deaths involving sepsis across 195 GBD causes of death, creating a comprehensive mortality envelope (ie, overall set) for non-infectious and infectious sepsis deaths. In the second modelling step, sepsis deaths were subdivided into 22 infectious syndromes using mixed-effects logistic regression; 11 had bacterial aetiologies relevant to AMR burden estimation. This step allocated sepsis deaths to syndromes by age, sex, location, and year, providing a detailed framework to analyse the impact of AMR across pathogens and syndromes.

In modelling steps three and four, pathogen-specific case-fatality ratios and pathogen distribution models were developed to link disease incidence with deaths. Case-fatality ratios results were then used to infer cases for pathogens from mortality-only datasets with useful pathogen distribution data. Pathogen distribution models estimated distributions for each infectious syndrome by age, year, and location. To handle diverse data, a multinomial estimation approach integrated covariates and Bayesian priors. Pathogen distributions included bacterial, viral, fungal, and parasitic pathogens whereas AMR burden calculations focused solely on clinically relevant bacteria with sufficient data.

In modelling steps five to seven, the prevalence of resistance was assessed across 84 pathogen-antibiotic combinations selected based on clinical relevance and data availability, with the exception of tuberculosis, for which existing GBD 2021 estimates were used.[13] National antibiotic consumption was modelled using data from surveys, pharmaceutical sales, and international health organisations, combined through geostatistics and an ensemble spatiotemporal Gaussian process regression model.[14] Resistance patterns were estimated using microbiology data, which included marginal frequencies and co-occurrences of resistance across antibiotics. A multinomial distribution approach ensured consistency, even with noisy or inconsistent data.[15] Additional covariates for each pathogen–drug combination were used from the GBD 2021 (appendix 1 pp 97–103). A two-stage spatiotemporal modelling framework, comprising a stacked ensemble model and Gaussian process regression, was used to estimate resistance prevalence for all location-years (1990–2021).

See Online for appendix 1

For the **global database for tracking antimicrobial resistance country self-assessment survey** see https://amrcountryprogress.org/#/visualization-view

For the **WHO AMR national action plan library** see https://www.who.int/teams/surveillance-prevention-control-AMR/national-action-plan-monitoring-evaluation/library-of-national-action-plans

	Deaths (count)						DALYs (thousands)					
	Associated with AMR			Attributable to AMR			Associated with AMR			Attributable to AMR		
	1990	2019	2021	1990	2019	2021	1990	2019	2021	1990	2019	2021
Infectious syndrome												
Infections of bones joints and related organs	176 (143–211)	804 (632–999)	841 (684–1080)	40 (32–51)	199 (154–250)	208 (167–260)	31 (24–41)	180 (134–239)	190 (140–263)	8 (6–11)	51 (37–67)	54 (39–75)
Peritoneal and intra-abdominal infections	9010 (7310–11 500)	19 700 (17 300–22 100)	20 000 (17 700–23 300)	206 (1590–2660)	4850 (4180–5770)	4950 (420–5980)	320 (262–408)	685 (597–785)	681 (590–785)	73 (58–94)	170 (144–201)	169 (144–202)
Bloodstream infections	129 000 (109 000–150 000)	163 000 (139 000–189 000)	161 000 (136 000–186 000)	30 200 (24 100–36 900)	41 000 (34 600–48 700)	40 400 (33 800–48 400)	8940 (7260–10 700)	9150 (7340–11 200)	8870 (7100–10 800)	2100 (1630–2640)	2280 (1820–2830)	2210 (1740–2730)
Diarrhoea	33 500 (23 700–46 200)	13 400 (10 000–17 400)	11 200 (8150–15 600)	6470 (4070–9670)	2710 (1890–3850)	2310 (1620–3360)	2740 (1900–3800)	1030 (715–1390)	852 (558–1180)	527 (323–784)	204 (143–284)	170 (111–239)
Endocarditis	3490 (2890–4250)	3050 (2550–3650)	2960 (2560–3540)	802 (635–998)	767 (641–923)	746 (613–891)	118 (94–143)	128 (104–155)	120 (102–144)	27 (21–34)	32 (26–40)	30 (25–37)
Lower respiratory infections	173 000 (137 000–211 000)	147 000 (129 000–167 000)	121 000 (103 000–138 000)	37 300 (27 500–47 800)	36 000 (30 600–43 800)	30 100 (25 300–37 400)	12 600 (9820–15 800)	7820 (6620–9080)	5780 (4830–6770)	2660 (1910–3460)	1860 (1520–2310)	1400 (1150–1760)
Meningitis	12 600 (9440–16 000)	9440 (7670–11 400)	8270 (6660–10 000)	2530 (1760–3430)	2040 (1610–2460)	1800 (1440–2190)	1020 (761–1310)	703 (559–868)	599 (471–742)	205 (141–281)	151 (118–182)	130 (101–163)
Sexually transmitted infections	..	..	..	..	..	..	1 (1–4)	3 (2–7)	3 (2–7)	0 (0–0)	0 (0–1)	0 (0–1)
Infections of the skin and subcutaneous systems	5760 (4870–6590)	10 000 (8780–11 600)	9900 (8340–11 600)	1280 (1020–1530)	2300 (1980–2690)	2280 (1940–2680)	244 (206–296)	470 (393–546)	474 (404–562)	57 (46–72)	119 (100–143)	121 (103–149)
Tuberculosis	177 (47–501)	12 100 (3590–26 700)	12 200 (3590–29 100)	56 (4–250)	3750 (617–11 600)	3860 (505–12 200)	8 (2–22)	551 (168–1200)	543 (164–1270)	3 (0–11)	158 (25–566)	156 (23–577)
Typhoid fever, paratyphoid fever, and invasive non-typhoidal *Salmonella*	9120 (4600–15 500)	12 900 (6890–22 200)	11 700 (6210–20 100)	1030 (429–2120)	1530 (657–2780)	1400 (620–2600)	725 (363–1250)	1010 (529–1760)	914 (470–1600)	82 (34–169)	120 (51–218)	108 (48–201)
Urinary tract infections and pyelonephritis	9320 (7830–11 300)	20 100 (17 000–23 400)	20 400 (17 700–24 500)	2050 (1630–2440)	4790 (3960–5600)	4880 (4160–5810)	306 (258–352)	596 (502–688)	593 (513–707)	67 (53–79)	141 (117–163)	141 (120–169)
Pathogen												
Acinetobacter baumannii	35 300 (32 300–38 600)	40 600 (36 600–45 300)	37 600 (33 100–42 000)	11 000 (9740–12 900)	13 300 (11 500–15 000)	12 300 (10 500–14 500)	2090 (1850–2380)	1950 (1680–2260)	1740 (1500–2030)	653 (573–783)	636 (537–744)	568 (476–676)
Citrobacter spp	3860 (3150–4870)	4760 (3910–5770)	4520 (3770–5320)	976 (791–1250)	1210 (990–1540)	1180 (956–1420)	268 (214–349)	279 (216–349)	260 (204–325)	68 (53–89)	72 (56–93)	68 (53–85)
Enterobacter spp	8980 (8110–10 200)	9770 (8340–11 300)	9190 (7700–10 700)	2310 (2020–2670)	2620 (2220–3100)	2460 (2040–2930)	565 (501–654)	492 (396–581)	448 (368–527)	147 (126–171)	135 (108–162)	124 (99–149)
Enterococcus faecalis	3520 (3050–4290)	7380 (6620–8570)	7260 (6440–8350)	583 (373–884)	1200 (902–1690)	1180 (850–1610)	144 (125–173)	258 (230–299)	247 (215–279)	24 (15–36)	40 (29–56)	38 (26–52)
Enterococcus faecium	3250 (2780–3790)	6640 (5880–7490)	6800 (5990–7710)	552 (404–719)	1370 (1140–1770)	1430 (1130–1750)	193 (165–226)	309 (264–365)	310 (265–361)	33 (23–43)	63 (50–81)	64 (49–80)
Escherichia coli	56 100 (44 600–68 400)	55 200 (48 900–60 900)	52 500 (45 900–58 100)	11 700 (8930–15 400)	12 800 (10 700–14 800)	12 300 (10 300–14 300)	3960 (3030–4910)	2900 (2390–3360)	2630 (2190–3040)	832 (604–1130)	677 (549–820)	621 (501–731)
Haemophilus influenzae	5030 (2360–9160)	3080 (1970–5110)	3190 (2350–4660)	925 (364–1870)	500 (295–875)	542 (379–793)	396 (187–729)	194 (124–313)	197 (144–281)	73 (29–148)	31 (19–53)	34 (23–50)

(Table 1 continues on next page)

	Deaths (count)						DALYs (thousands)					
	Associated with AMR			Attributable to AMR			Associated with AMR			Attributable to AMR		
	1990	2019	2021	1990	2019	2021	1990	2019	2021	1990	2019	2021
(Continued from previous page)												
Klebsiella pneumoniae	56 500 (47 600–64 700)	57 100 (49 300–65 500)	52 800 (45 200–60 000)	12 400 (9810–15 000)	14 800 (12 500–17 400)	13 800 (11 600–16 700)	3970 (3290–4630)	3250 (2690–3780)	2880 (2360–3400)	871 (686–1060)	845 (686–1020)	755 (608–927)
Morganella spp	3190 (2700–3800)	4070 (3500–4720)	3990 (3500–4580)	694 (579–848)	833 (676–1030)	816 (651–974)	191 (151–241)	199 (158–259)	191 (155–236)	42 (32–54)	41 (31–53)	40 (30–50)
Mycobacterium tuberculosis	177 (47–501)	12 100 (3590–26 700)	12 200 (3590–29 100)	58 (6–225)	3630 (598–12 300)	3540 (586–12 100)	8 (2–22)	551 (168–1200)	543 (164–1270)	3 (0–11)	153 (26–624)	159 (21–557)
Proteus spp	3580 (3050–4160)	6570 (5690–7430)	6650 (5750–7500)	620 (478–772)	1160 (971–1420)	1170 (984–1390)	177 (146–210)	276 (231–314)	276 (233–311)	31 (23–39)	50 (40–61)	50 (40–62)
Pseudomonas aeruginosa	30 400 (25 000–35 300)	37 500 (32 800–43 700)	34 900 (30 100–40 000)	8660 (7080–10 300)	11 400 (9910–13 500)	10 700 (9000–13 100)	2000 (1650–2370)	1930 (1640–2270)	170 (1430–2000)	570 (463—684)	587 (496–707)	522 (430–639)
Non-typhoidal *Salmonella*	1730 (620–3360)	1670 (875–2710)	1450 (698–2320)	193 (45–440)	184 (62–368)	160 (52–328)	144 (49–284)	136 (67–231)	117 (52–202)	16 (4–34)	14 (5–28)	12 (4–24)
Salmonella enterica serovar Paratyphi	830 (240–1920)	2800 (1200–5520)	2610 (1080–4990)	125 (38–296)	421 (147–837)	395 (144–807)	63 (18–147)	209 (87–408)	194 (80–368)	9 (3–22)	32 (11–61)	29 (10–58)
Salmonella enterica serovar Typhi	7890 (3800–13 900)	9000 (4070–15 800)	8150 (3700–15 000)	864 (346–1800)	987 (387–2060)	895 (361–1870)	634 (303–1130)	725 (322–1290)	651 (295–1210)	69 (28–145)	79 (32–168)	71 (29–149)
Serratia spp	8970 (7670–10 700)	9140 (7400–11 000)	8810 (7060–10 900)	2210 (1870–2680)	2480 (2030–3050)	2370 (1890–2900)	637 (532–774)	568 (438–710)	540 (409–684)	157 (131–194)	156 (120–193)	146 (112–185)
Shigella spp	3810 (1840–7470)	2850 (1700–4800)	2530 (1480–4360)	419 (148–949)	317 (145–605)	281 (122–569)	325 (157–646)	239 (142–415)	212 (122–371)	36 (12–82)	26 (12–50)	23 (10–46)
Staphylococcus aureus	28 200 (21 600–34 000)	50 100 (44 300–58 100)	49 500 (43 100–56 200)	6320 (4170–8500)	12 300 (10 200–14 900)	12 200 (10 200–14 500)	1740 (1340–2130)	2380 (2020–2750)	2250 (1920–2600)	392 (264–525)	588 (486–709)	559 (462–658)
Group A *Streptococcus* (*Streptococcus pyogenes*)	2790 (2370–3270)	3280 (2810–3720)	3090 (2660–3630)	130 (70–177)	153 (86–212)	144 (83–202)	212 (177–253)	207 (173–245)	187 (155–223)	10 (6–14)	11 (7–14)	10 (6–14)
Group B *Streptococcus* (*Streptococcus agalactiae*)	5320 (4100–7240)	8920 (6980–11 000)	9000 (7030–11 000)	603 (369–982)	1030 (676–1440)	1040 (673–1530)	432 (329–590)	661 (506–824)	662 (504–831)	49 (30–80)	77 (50–108)	77 (49–115)
Streptococcus pneumoniae	115 000 (90 000–142 000)	78 800 (68 700–89 300)	62 800 (53 400–71 000)	22 500 (15 800–29 200)	17 100 (13 500–21 700)	13 800 (10 800–17 700)	8850 (6850–11 100)	4610 (3920–5300)	3370 (2770–3950)	1720 (1200–2250)	968 (745–1260)	717 (539–927)
Neisseria gonorrhoeae	..	..	..	..	..	..	1 (1–4)	3 (2–7)	3 (2–7)	0 (0–0)	0 (0–1)	0 (0–1)
Total*	385 000 (317 000–457 000)	411 000 (365 000–470 000)	380 000 (332 000–426 000)	83 900 (66 200–103 000)	99 800 (86 800–119 000)	92 800 (78 300–111 000)	27 000 (21 900–32 700)	22 300 (19 100–25 700)	22 300 (19 100–25 700)	5800 (4540–7330)	5290 (4380–6350)	4690 (3880–5630)

Data in parentheses are 95% uncertainty intervals. Mortality and disability estimates were aggregated across drugs, accounting for the co-occurrence of resistance to multiple drugs. The fatal burden of *Neisseria gonorrhoeae* and STIs were not estimated, therefore, only the DALY burden is presented. AMR=antimicrobial resistance. DALYs=disability-adjusted life-years. *Data in this row represent the sum of the infectious syndrome burdens or the sum of the pathogen burdens.

Table 1: **Overall AMR burden by infectious syndrome and pathogen in the WHO Eastern Mediterranean Region in 1990, 2019, and 2021**

In modelling steps eight and nine, the estimated relative risk of death for drug-resistant infections was compared with drug-sensitive infections. A modelling approach with the use of the Meta-Regression–Bayesian, Regularized, Trimmed was used and a two-stage nested mixed effects meta-regression model to determine relative risk by antibiotic class, pathogen, and infectious syndrome, assuming no variation by location or age. The same approach was used to estimate non-fatal excess risk, measured as increased hospital length of stay.

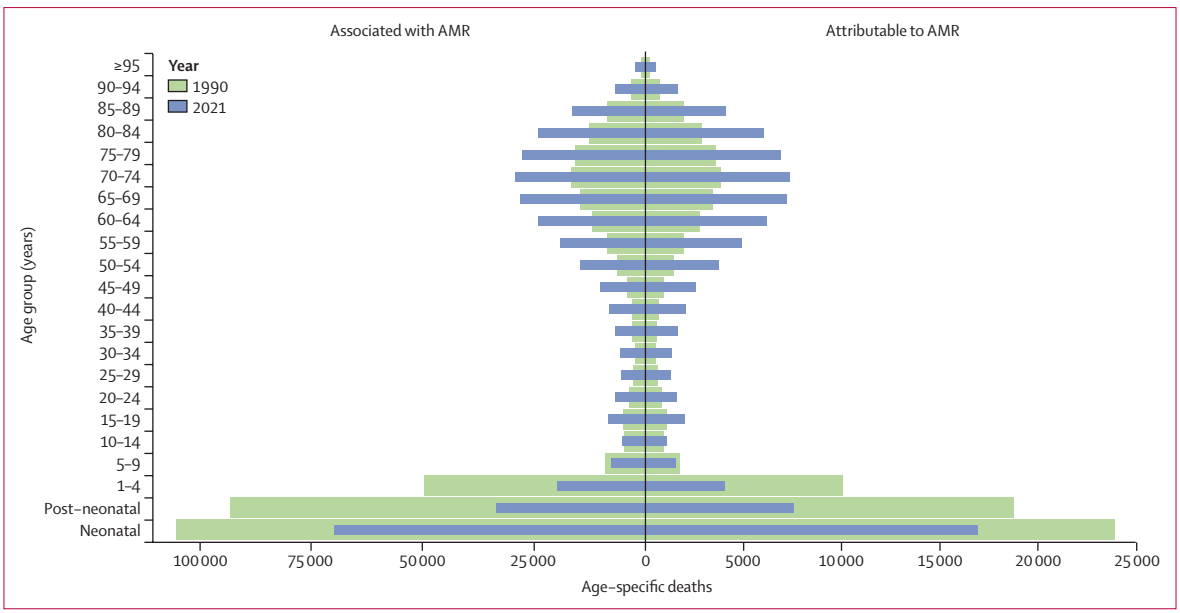

Figure 1: **Age-specific mortality for deaths attributable to and deaths associated with AMR in the WHO Eastern Mediterranean Region in 1990 and 2021**
AMR=antimicrobial resistance.

The final step quantified AMR burden using two counterfactual scenarios: replacing resistant infections with susceptible ones, and replacing them with no infection. Burden attributable to AMR was calculated by combining cause-specific deaths, sepsis fractions syndrome-specific contributions, pathogen-specific contributions, and population attributable fractions for resistance profiles. Years of life lost (YLLs) were estimated using standard life expectancy, whereas years lived with disability (YLDs) were derived from syndrome incidence, pathogen attribution and non-fatal population attributable fraction. For multidrug-resistant profiles, burdens were redistributed across individual antibiotic classes based on risk. The total DALYs were calculated by summing YLLs and YLDs, providing comprehensive estimates of AMR burden across drug-sensitive and drug-resistant counterfactuals. Additionally, a correlation analysis of AMR mortality rates was done using the Socio-demographic Index, a summary measure of income per capita, educational attainment, and total fertility rate.

AMR forecasting approach

The Institute for Health Metrics and Evaluation Future Health Scenarios framework[16] was used to forecast the burden of AMR from 2022 to 2050, integrating disease burden forecasts by cause, age, sex, and location with AMR trends. Forecasting involved calculating AMR population attributable fractions using historical AMR death data. A generalised ensemble model with 12 sub-models, based on annualised rates of change and meta-regression techniques, was employed to predict population attributable fractions for 19 level 2 GBD causes (appendix 2 p 1). The final ensemble forecast averaged these sub-models using weights derived from out-of-sample experiments, which were then applied to reference mortality forecasts to estimate future AMR attributable burden.

See Online for appendix 2

To compute the future AMR-attributable burden, mortality forecasts for 19 causes were multiplied by the projected AMR population attributable fractions, and the GBD reference life table was used to compute future YLLs. YLDs were estimated using the global YLL-to-YLD ratio for AMR deaths in 2019. Attributable DALYs were derived by summing YLLs and YLDs. For associated AMR burden, the ratio of associated to attributable deaths by cause in 2021 was calculated and applied to the forecasted AMR population attributable fractions to determine associated burden for each metric. More details are available in the appendix of the global AMR publication.[4]

Uncertainty analysis

Consistent with previously described GBD methods,[13] uncertainty was propagated from each step of the analysis into the final estimates of deaths and infections attributable to and associated with drug resistance by combining 100 draws for each location, sex, age, and year from the posterior distribution. For forecasting estimates, uncertainty intervals were derived from the 2·5th and 97·5th percentiles of distributions generated by propagating 500 draws through the multistage computational pipeline. The models were cross-validated for out-of-sample predictive validity.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or the writing of the report.

	Deaths (count)								DALYs (thousands)						Age-standardised mortality rate (per 100 000 population)*					
	Associated with AMR				Attributable to AMR				Associated with AMR			Attributable to AMR			Associated with AMR			Attributable to AMR		
	1990	2019	2021	2050	1990	2019	2021	2050	1990	2019	2021	1990	2019	2021	1990	2019	2021	1990	2019	2021
Afghanistan	20 200 (15 100–25 200)	23 700 (18 600–28 800)	21 900 (17 300–26 500)	33 500 (21 400–51 100)	4790 (3440–6140)	6120 (4570–7660)	5690 (4270–7120)	8490 (5290–13 000)	1390 (1060–1 80)	1550 (1230–1940)	1400 (1120–1760)	323 (226–420)	394 (289–499)	360 (263–457)	183 (139–226)	134 (106–162)	124 (99–149)	44 (32–57)	36 (27–44)	33 (25–41)
Bahrain	166 (139–194)	302 (242–361)	318 (252–383)	1460 (1140–1870)	45 (36–54)	80 (61–98)	83 (63–103)	357 (273–475)	8 (7–9)	11 (9–13)	11 (9–14)	2 (2–3)	3 (2–4)	3 (2–4)	107 (89–125)	60 (48–72)	58 (47–70)	28 (23–34)	16 (12–19)	15 (12–18)
Djibouti	470 (356–585)	862 (618–1110)	828 (590–1070)	210 (1450–3000)	109 (78–140)	209 (142–275)	200 (135–264)	480 (325–682)	34 (26–43)	43 (33–58)	40 (30–53)	8 (6–10)	10 (7–14)	9 (6–12)	175 (133–217)	139 (102–177)	130 (95–164)	42 (30–54)	34 (24–44)	31 (22–41)
Egypt	66 700 (57 700–75 700)	55 900 (51 100–60 700)	52 500 (42 600–62 400)	128 000 (95 100–161 000)	16 900 (13 900–19 900)	16 400 (14 400–18 500)	15 500 (12 50–18 500)	35 700 (25 800–45 500)	4410 (3760–5190)	2290 (2020–2590)	1950 (1600–2370)	1110 (885–1330)	672 (573–772)	574 (457–690)	175 (156–195)	107 (98–116)	100 (83–116)	45 (38–52)	32 (28–35)	29 (24–34)
Iran	28 800 (23 900–33 700)	27 900 (24 800–31 000)	25 400 (22 400–28 400)	65 900 (50 100–85 000)	6790 (5180–8400)	7630 (6470–8800)	6930 (5850–8010)	16 800 (12 600–21 400)	1950 (1610–2350)	840 (761–928)	711 (639–790)	453 (336–569)	230 (196–264)	194 (165–223)	75 (64–86)	42 (37–47)	37 (32–42)	18 (14–22)	12 (10–13)	10 (8–12)
Iraq	12 000 (9770–14 200)	13 400 (10 600–16 200)	12 800 (10 200–15 400)	28 000 (17 000–40 800)	2940 (2290–3580)	3630 (2830–4430)	3450 (2710–4180)	7150 (4270–10 800)	810 (663–990)	629 (514–771)	539 (440–661)	196 (150–243)	169 (132–207)	144 (113–176)	78 (64–91)	56 (44–68)	56 (45–67)	20 (15–24)	15 (12–19)	15 (12–18)
Jordan	1460 (1210–1700)	2150 (1760–2530)	2280 (1810–2740)	8060 (5710–10 700)	363 (278–447)	582 (467–697)	613 (480–747)	2030 (1400–2700)	94 (79–112)	93 (78–111)	92 (76–113)	23 (18–29)	25 (20–30)	25 (20–30)	68 (55–80)	36 (29–42)	35 (28–42)	17 (13–21)	10 (8–12)	9 (7–11)
Kuwait	373 (282–463)	606 (533–679)	598 (486–709)	3070 (2150–3970)	92 (67–116)	147 (125–169)	145 (115–174)	700 (478–920)	21 (17–28)	22 (19–24)	21 (17–25)	5 (4–7)	5 (4–6)	5 (4–6)	43 (33–52)	27 (23–31)	24 (20–29)	10 (8–13)	7 (5–8)	6 (5–7)
Lebanon	1630 (1240–2020)	2500 (2040–2970)	2470 (1980–2960)	4390 (3200–5720)	375 (272–477)	606 (468–743)	593 (452–733)	1010 (714–1360)	73 (57–93)	58 (49–68)	56 (47–67)	17 (12–21)	14 (11–17)	14 (11–17)	73 (56–91)	40 (33–48)	38 (31–46)	17 (12–22)	10 (8–12)	9 (7–11)
Libya	1590 (1260–1930)	2660 (2040–3280)	2390 (1770–3010)	6090 (4200–8490)	398 (300–496)	714 (529–899)	639 (463–816)	1520 (1020–2180)	91 (73–113)	100 (80–125)	81 (63–105)	23 (17–28)	27 (20–34)	22 (16–28)	59 (46–71)	58 (44–71)	51 (38–64)	15 (11–18)	16 (11–20)	14 (10–17)
Morocco	16 400 (12 700–20 100)	13 300 (10 400 16 100)	12 700 (10 000–15 400)	22 900 (16 900–29 500)	3390 (2500–4270)	3080 (2370–3800)	2960 (2290–3620)	5140 (3720–6780)	1060 (833–1360)	414 (335–513)	379 (306–469)	213 (153–273)	96 (74–119)	88 (68–109)	76 (60–92)	45 (36–55)	42 (34–51)	16 (12–20)	10 (8–13)	10 (8–12)
Oman	795 (600–991)	726 (581–871)	657 (513–801)	2840 (2010–3800)	216 (161–270)	187 (144–231)	170 (128–211)	700 (480–946)	48 (37–61)	31 (26–38)	27 (22–34)	13 (10–16)	8 (6–10)	7 (5–9)	78 (58–97)	45 (36–54)	39 (31–47)	21 (15–26)	12 (9–14)	10 (8–12)
Pakistan	149 000 (121 000–177 000)	176 000 (150 000 203 000)	161 000 (134 000–187 000)	262 000 (191 000–339 000)	30 700 (23 900–37 500)	42 600 (34 600–50 700)	39 700 (31 000–48 300)	63 200 (45 400–84 700)	10 900 (8830–13 300)	11 100 (9280–13 300)	9690 (8020–11 700)	2190 (1660–2720)	2610 (2070–3140)	2330 (1810–2850)	135 (111–159)	109 (94–125)	100 (84–116)	29 (23–35)	27 (22–32)	25 (20–31)
Palestine	1190 (912–1460)	1180 (994–1360)	1150 (956–1340)	3100 (2310–4090)	294 (214–373)	310 (250–369)	300 (241–360)	777 (563–1050)	69 (55–88)	49 (41–58)	45 (38–54)	17 (12–22)	13 (10–16)	12 (9–14)	90 (68–112)	53 (45–61)	50 (41–58)	23 (16–29)	14 (11–17)	13 (10–16)
Qatar	81 (62–100)	232 (172–293)	222 (159–285)	2510 (1810–3340)	21 (15–27)	58 (42–74)	56 (40–72)	587 (418–806)	4 (3–5)	11 (9–14)	10 (8–13)	1 (1–1)	3 (2–4)	3 (2–3)	81 (63–99)	32 (24–40)	32 (24–41)	21 (16–26)	8 (6–10)	8 (6–10)
Saudi Arabia	7980 (6230–9730)	8670 (7050–10 300)	8620 (6780–10 500)	35 600 (27 200–45 500)	2030 (1560–2500)	2290 (1830–2750)	2260 (1750–2770)	8690 (6520–11 100)	484 (385–607)	384 (312–473)	383 (300–489)	124 (94–153)	103 (80–126)	102 (75–128)	94 (73–116)	57 (48–66)	52 (43–61)	24 (18–30)	15 (12–17)	13 (11–16)

(Table 2 continues on next page)

	Deaths (count)						DALYs (thousands)						Age-standardised mortality rate (per 100 000 population)*					
	Associated with AMR			Attributable to AMR			Associated with AMR			Attributable to AMR			Associated with AMR			Attributable to AMR		
	1990	2019	2021	1990	2019	2021	1990	2019	2021	1990	2019	2021	1990	2019	2021	1990	2019	2021
(Continued from previous page)																		
Somalia	17 700 (13 300–22 100)	30 600 (22 700–38 400)	29 200 (21 200–37 200)	4100 (2880–5310)	7390 (4880–9890)	7130 (4500–9750)	1350 (1040–1750)	2100 (1610–2750)	1980 (1500–2620)	308 (212–404)	498 (344–652)	473 (315–630)	277 (217–336)	265 (198–332)	244 (177–312)	66 (48–84)	67 (39–94)	62 (34–90)
Sudan	28 100 (20 900–35 400)	16 100 (11 500–20 800)	14 600 (10 500–18 600)	6730 (4760–8700)	4380 (3110–5660)	3940 (2840–5030)	2140 (1630–2800)	906 (671–1220)	775 (582–1030)	504 (348–661)	245 (167–323)	208 (147–270)	131 (102–160)	65 (48–82)	60 (45–76)	32 (24–41)	18 (13–23)	16 (12–21)
Syria	6260 (4820–7700)	7600 (5760–9440)	5920 (4360–7490)	1400 (1030–1780)	1960 (1430–2480)	1520 (1090–1940)	386 (301–496)	293 (228–377)	180 (139–232)	85 (61–110)	76 (53–98)	46 (33–59)	76 (60–92)	72 (55–88)	57 (43–71)	18 (13–22)	18 (14–23)	14 (11–18)
Tunisia	3440 (2560–4330)	4400 (3080–5720)	4270 (3030–5500)	824 (592–1060)	1120 (767–1460)	1070 (747–1390)	202 (153–268)	125 (94–166)	117 (88–155)	48 (33–63)	32 (22–42)	30 (21–38)	57 (44–71)	40 (28–51)	36 (26–47)	14 (10–18)	10 (7–13)	9 (6–12)
United Arab Emirates	416 (313–519)	1130 (868–1390)	970 (770–1170)	112 (83–141)	275 (205–346)	236 (184–288)	22 (18–29)	44 (35–55)	37 (30–45)	6 (4–8)	11 (8–14)	9 (7–11)	82 (62–101)	75 (60–90)	48 (39–58)	22 (16–28)	18 (14–22)	12 (9–14)
Yemen	17 600 (13 300–21 800)	15 300 (11 400–19 100)	13 400 (10 100–16 700)	3930 (2820–5050)	3700 (2640–4770)	3270 (2370–4180)	1390 (1090–1780)	914 (706–1180)	759 (598–964)	308 (219–398)	220 (152–288)	184 (132–236)	122 (94–151)	78 (58–97)	71 (52–89)	28 (21–36)	19 (14–24)	18 (12–22)
Eastern Mediterranean Region	385 000 (317 000–457 000)	411 000 (365 000–470 000)	380 000 (332 000–426 000)	83 900 (66 200–103 000)	99 800 (86 800–119 000)	92 800 (78 300–111 000)	27 000 (21 900–32 700)	22 300 (19 100–25 700)	19 600 (16 400–22 600)	5800 (4540–7330)	5290 (4380–6350)	4690 (3880–5630)	102 (84–121)	57 (50–65)	51 (44–57)	22 (18–27)	14 (12–16)	12 (10–15)

Data in parentheses are 95% uncertainty intervals. Burden is expressed in counts and age-standardised rates per 100 000 person-years. AMR=antimicrobial resistance. DALYs=disability-adjusted life-years.

Table 2: **Overall AMR burden by country in the WHO Eastern Mediterranean Region in 1990, 2019, and 2021**

Results

AMR burden by infections and infectious syndromes

In the EMR in 1990, there were an estimated 1·26 million (95% uncertainty interval [UI] 1·17–1·35) deaths with sepsis involving at least one of the 11 infectious syndromes as an underlying or intermediate cause of death (table 1). The number of deaths decreased to 1·07 million (0·96–1·18) deaths in 2019 before increasing to 1·77 million (1·61–1·91) deaths in 2021 as a result of the COVID-19 pandemic. In children younger than 5 years, deaths with sepsis decreased from 780 000 deaths (716 000–844 000) in 1990 to 403 000 deaths (332 000–475 000) in 2019 and to 327 000 deaths (269 000–400 000) in 2021; conversely, in people aged 5 years and older, deaths with sepsis increased from 479 000 deaths (446 000–526 000) in 1990 to 672 000 deaths (624 000–725 000) in 2019 to 1·44 million (1·32–1·53) deaths in 2021; of which 57·8% of deaths in 2021 were due to COVID-19. Many of those deaths were associated with both susceptible and resistant bacteria. Among them, lower respiratory tract and thorax infections accrued the largest fatal burden in 1990, with 304 000 deaths (266 000–348 000), accounting for 24·1% of all deaths caused by infectious syndromes. In 2019 and 2021, however, leading infectious syndrome were bloodstream infections with 305 000 deaths (266 000–356 000) and 301 000 deaths (261 000–347 000), respectively, accounting for 28·4% and 17·1% of all infectious syndromes in 2019 and 2021, respectively.

A substantial fraction of deaths from infectious syndromes were linked to resistant bacteria; more specifically, five of every eight bacterial infection deaths in the EMR in 2021 were associated with AMR (380 000 deaths [95% UI 332 000–426 000]; table 1). Of these, 92 800 deaths (78 300–111 000) were attributable to AMR. 19·6 million (16·4–22·6) and 4·7 million (3·9–5·6) estimated DALYs were associated with and attributable to AMR in 2021, respectively. This can be compared with 2019, in which there were an estimated 99 800 deaths (86 800–119 000) attributable to and 411 000 deaths (365 000–470 000) associated with AMR, and to 1990 with estimated 385 000 deaths (317 000–457 000) associated with and 83 900 deaths (66 200–103 000) attributable to AMR. In 2021, among respiratory infection deaths, a total of 121 000 deaths (103 000–138 000) were associated with and 30 100 deaths (25 300–37 400) were attributable to AMR. Similarly, among bloodstream infection deaths, 161 000 deaths (136 000–186 000) were associated with and 40 400 deaths (33 800–48 400) were attributable to AMR in 2021. Together with intra-abdominal and urinary tract infections, these four syndromes were responsible for 25·5% and 18·2% of associated deaths (and 5·7% and 4·5% of attributable deaths) in the region in 1990 and 2021, respectively (table 1).

AMR burden changes from 1990–2021 were most evident when estimates were divided into two age groups: people aged younger than 5 years and people

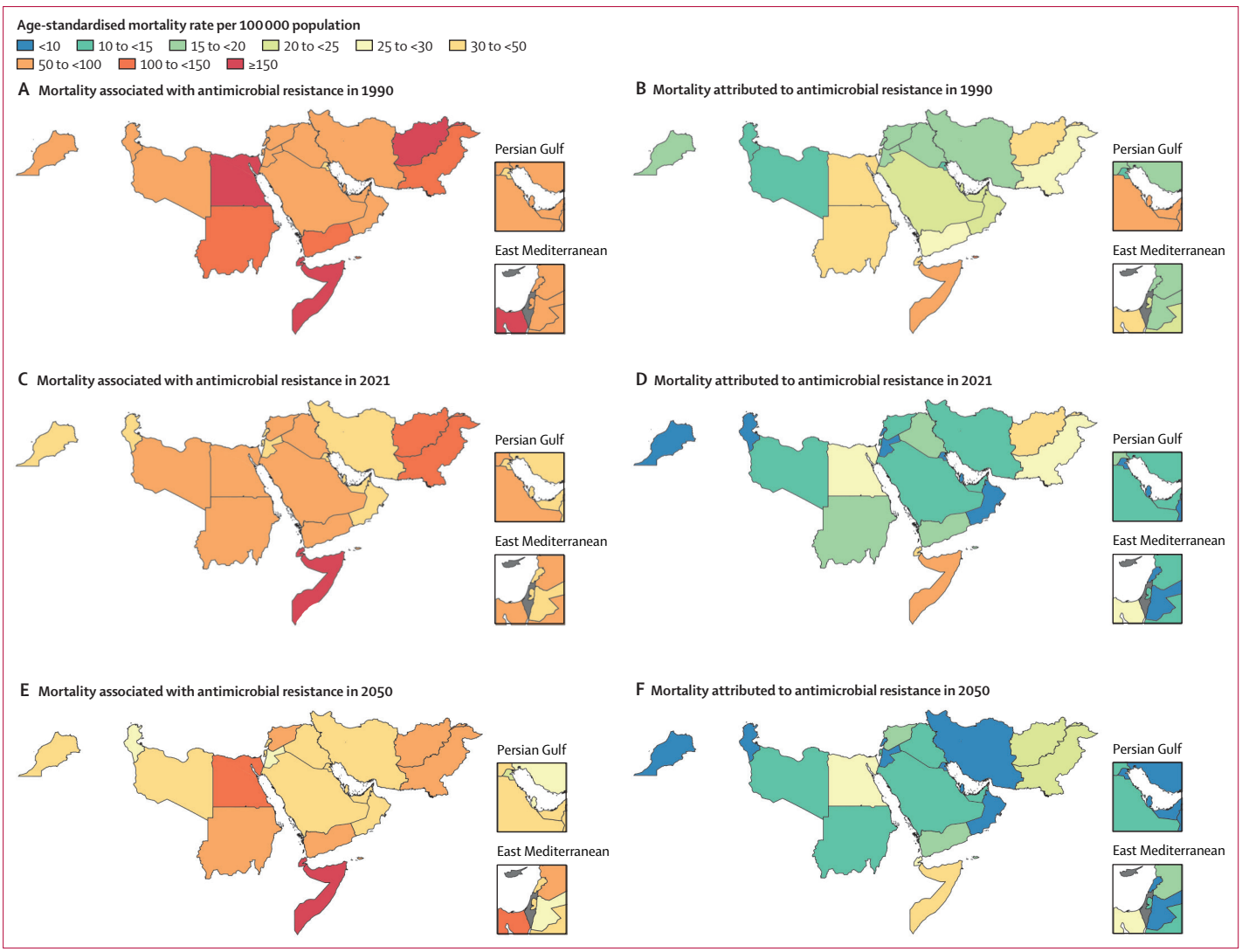

Figure 2: **Age-standardised mortality rates per 100 000 population for deaths associated with and attributable to antimicrobial resistance in the WHO Eastern Mediterranean Region in 1990 (A, B), 2021 (C, D) and 2050 (E, F)**

aged 5 years and older. In 1990, in children under the age of 5 years, there were 248 000 deaths (95% UI 199 000–303 000) associated with and 52 900 deaths (40 700–67 600) attributable to AMR; conversely, in people aged 5 years and older, there were an estimated 137 000 deaths (118 000–156 000) associated with and 31 000 deaths (25 400–36 400) attributable to AMR. In 2021, there were 123 000 deaths (94 400–152 000) associated with AMR and 28 600 deaths (22 100–35 800) attributable to AMR in children younger than 5 years of age compared with 257 000 deaths (228 000–290 000) deaths attributable to AMR and 64 200 deaths (54 900–76 600) associated with AMR in people aged 5 years and older. In people younger than 5 years, AMR-associated mortality decreased by 50·0% (38·2–62·0) and AMR-attributable mortality decreased by 45·2% (29·3–60·5) between 1990 and 2021, while in people aged older than 5 years, AMR-associated mortality increased by 88·5% (60·4–120·9) and AMR-attributable mortality increased by 108·7% (62·3–160·7), and in adults aged 70 years or older AMR-associated mortality increased by 85·7% (57·0–115·7) and AMR-attributable mortality increased by 103·6% (55·9–141·7) over the study period (ie, 1990–2021). Figure 1 shows AMR burden by age group, with a shift evident from younger to older populations between 1990 and 2021.

AMR burden by location in the EMR

When analysing the resistance burden by country, Pakistan was identified as the country with the highest absolute burden of AMR for all pathogens, with 31 000 deaths (95% UI 24 000–37 500) attributable to and 149 000 deaths (121 000–177 000) associated with AMR in 1990, and 40 000 deaths (31 000–48 000) attributable to

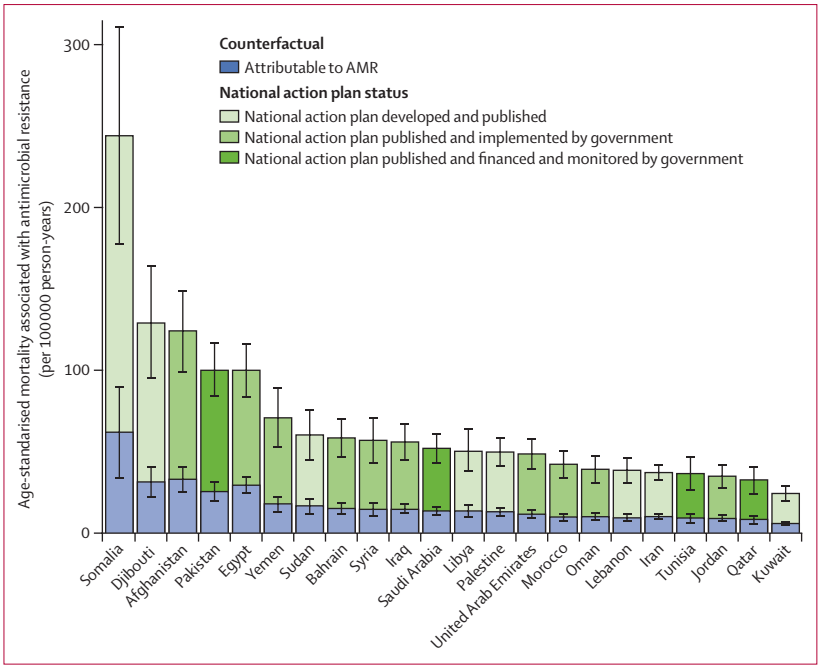

Figure 3: **Age-standardised mortality rate associated with and attributable to AMR by national action plan status for the countries in the WHO Eastern Mediterranean Region**

Rates per 100 000 population are coloured according to two-dimensional national action plan status: (1) the highest self-reported government engagement with the national action plan between 2018 and 2021 and (2) whether the national action plan was published online as reported in surveys or the WHO national action plan website. Error bars indicate 95% uncertainty intervals. Estimates were aggregated across drugs, accounting for the co-occurrence of resistance to multiple drugs. AMR=antimicrobial resistance.

and 161 000 deaths (134 000–187 000) associated with AMR in 2021 (table 2). Conversely, Qatar had the lowest burden of absolute mortality, with 21 deaths (15–27) attributable to AMR and 81 deaths (62–100) associated with AMR in 1990, and 56 deaths (40–72) attributable to AMR and 222 deaths (159–285) associated with AMR in 2021 (table 2). Burden by country and age group are shown in appendix 1 (p 78).

Since counts depend on country size, between-country analysis can be done by using age-standardised mortality rates per 100 000 population (appendix 3 pp 1–38). In the EMR, Somalia had the highest age-standardised mortality rates: in 1990, 65·9 deaths (95% UI 48·3–83·5) per 100 000 population were attributable to and 276·5 deaths (216·3–336·5) per 100 000 population were associated with AMR and in 2021, 62·1 deaths (33·8–90·4) per 100 000 population attributable to and 244·4 deaths (177·3–311·5) per 100 000 population were associated with AMR. Afghanistan had the second-highest burden and Egypt had the third-highest burden in the region (table 2). Conversely, the lowest age-standardised mortality rates were observed in Qatar: in 1990, 20·9 deaths (15·6–26·4) per 100 000 population were attributed to AMR and 81·1 deaths (63·4–98·9) per 100 000 population were associated with AMR and in 2021, 8·1 deaths (5·9–10·2) per 100 000 population were attributable to AMR and 32·5 deaths (24·1–40·9) per 100 000 population were associated with AMR (table 2; appendix 1 p 80).

Detailed cross-country comparisons of age-standardised mortality rates show that most EMR countries with the highest AMR burden were in eastern sub-Saharan Africa and south Asia (in accordance with GBD region breakdown), with additional considerable contribution from Afghanistan (table 2, figure 2). Five countries had an age-standardised mortality rate attributable to AMR higher than 25 deaths per 100 000 population in 2021 (table 2, figure 2); in addition to Somalia, which had the highest burden, these were Afghanistan, Djibouti, Egypt, and Pakistan; 33·0 deaths (95% UI 25·3–40·7) per 100 000 population, 31·2 deaths (21·8–40·7) per 100 000 population, 29·3 (24·3–34·4) deaths per 100 000 population, and 25·4 deaths (24·3–34·4) per 100 000 population (table 2, figure 2). These countries also had an age-standardised mortality rate associated with AMR higher than 65 deaths per 100 000 population in 2021 (table 2, figure 2). Kuwait had the lowest age-standardised attributable mortality rate in 2021 (attributable 5·8 deaths [4·6–6·9] per 100 000 population attributable to AMR; 24·1 deaths [19·5–28·6] per 100 000 population associated with AMR), followed by Qatar (8·1 deaths [5·9–10·2] per 100 000 population attributable to AMR; 32·5 deaths [24·1–40·9] per 100 000 population associated with AMR) and Tunisia (9·1 deaths [6·4–11·8] per 100 000 population attributable to AMR; 36·5 deaths [26·2–46·8] per 100 000 population associated with AMR; table 2; appendix 3 p 6).

Figure 3 compares AMR mortality rates with each country's self-reported progress on a national action plan. EMR countries with government-endorsed and funded national action plans generally fared better (ie, had lower mortality rates than countries without government-endorsed and funded national action plans), particularly compared with Somalia, whose published national action plan remains unapproved and unfunded. Additionally, a correlation between age-standardised mortality rates associated with AMR and the Socio-demographic Index shows a strong negative association (correlation coefficient r=–0·82 [95% –0·92 to –0·6]; appendix 1 p 81). Generally, countries with a lower Socio-demographic Index had a larger AMR death burden in 2021 than countries with a higher Socio-demographic Index. The analogous pattern is observed when mortality associated with AMR was analysed.

See Online for appendix 3

AMR burden by pathogens and bacteria–drug combinations

Three pathogens can be linked to more than 50 000 AMR-associated deaths in the EMR in both 1990 and 2021, making them the top generators of burden in the region: *Streptococcus pneumoniae* (115 000 deaths [95% UI 90 000–142 000] in 1990; 62 800 deaths [53 400–71 000] in

2021), *Klebsiella pneumoniae* (56 500 deaths [47 600–64 700] in 1990; 52 800 deaths [45 200–60 000] in 2021), and *Escherichia coli* (56 100 deaths [44 600–68 400] in 1990; 52 500 deaths [45 900–58 100] in 2021; table 1). Additionally, two additional Gram-negative pathogens were each responsible for more than 30 000 deaths associated with AMR: *Acinetobacter baumannii* (35 300 deaths [32 300–38 600] in 1990; 37 600 deaths [33 100–42 000] in 2021) and *Pseudomonas aeruginosa* (30 400 deaths [25 000–35 300] in 1990; 34 900 deaths [30 100–40 000] in 2021). A substantial rise in the AMR burden due to *Staphylococcus aureus* was observed between 1990 (28 200 deaths [21 600–34 000]) and 2021 (49 500 deaths [43 100–56 200]). In total, these six pathogens were responsible for 75 000 deaths attributable to AMR and 290 000 deaths associated with AMR in the region in 2021, which accounted for 80·1% and 76·3% of the overall burden, respectively (table 1, figures 2, 3).

When leading species in different countries were considered, in 2021 in Pakistan, which was the country with the highest absolute burden, the highest mortality counts were observed for *K pneumoniae* resistant to any of the appraised antimicrobials for the attributable burden (7000 deaths [95% UI 5600–8400]) and *E coli* for associated burden (24 800 deaths [20 400–29 200]). This is in contrast with the 1990s, when *S pneumoniae* was the predominant pathogen with regard to attributable and associated AMR mortality in the country. However, many countries in the region do not follow this pattern. For example, *S pneumoniae* remained the leading resistant pathogen for attributable and associated AMR burden in both 1990 and 2021 in Somalia and Egypt, while *S aureus* became the pathogen causing the largest attributable and associated burden in 2021 in Bahrain, Jordan, Iraq, Kuwait, Lebanon, Libya, Oman, Palestine, Qatar, and Saudi Arabia. The highest burden attributable to AMR in Djibouti, Sudan, and United Arab Emirates was due to resistant *A baumannii*. Thus, while *S pneumoniae* had the highest regional AMR-associated burden in 2021, it was the leading cause of AMR-associated burden in only 31·8% of countries.

When specific pathogen–drug combinations were considered, in 2021, methicillin-resistant *S aureus* was shown to contribute to the highest burden in 13 countries (more than half of countries in the whole region) for deaths attributable to AMR (appendix 1 pp 127–128) and in nine countries (40·0% of the whole region) for deaths associated with AMR in 2021 (appendix 1 pp 127–128). Other leading pathogen–drug combinations for attributable burden in 2021 were *S pneumoniae* resistant to carbapenems (five countries), multidrug-resistant *M tuberculosis* (two countries), and *A baumannii* resistant to carbapenems (two countries). For associated burden, we also observed *K pneumoniae* resistant to the combination of β-lactams and β-lactam inhibitors as a leading pathogen–drug combination in three countries, aminopenicillin-resistant *E coli* in three countries, macrolide-resistant *S aureus* in two countries, trimethoprim-sulfametoxazole resistant *S pneumoniae* in two countries, and *A baumannii* resistant to third-generation cephalosporins, and *S pneumoniae* resistant to carbapenems and to beta-lactams and beta-lactam inhibitors in one country each. This contrasts with the early 1990s, when carbapenem-resistant and trimethoprim-sulfamethoxazole-resistant *S pneumoniae* accounted for the highest attributable and associated AMR burden, respectively. The analogous distribution was evident when comparing DALYs for pathogen–drug combinations across both counterfactual scenarios.

AMR burden forecasts in the EMR

By 2050, the number of deaths attributable to AMR in the EMR is forecasted to reach 187 000 (95% UI 157 000–223 000), with 752 000 AMR-associated deaths (629 000–879 000) projected. Cumulatively, from 2025 to 2050, the total number of deaths attributable to AMR is expected to be 3·5 million (2·9–4·3), and those associated with AMR 14·2 million (11·8–16·7). Although all-age mortality rates are rising, age-standardised rates are projected to decline slightly, reflecting ageing and demographic shifts. The DALYs attributable to AMR in the EMR are also forecasted to increase from 5·0 million (3·9–6·4) in 2022 to 5·5 million (4·3–7·1) in 2050. However, the all-age DALY rate attributable to AMR is expected to decline modestly, decreasing from 451 DALYs per 100 000 population (76–2060) in 2022 to 429 DALYs per 100 000 (159–1140) in 2050. The decline in mortality rate reflects demographic changes, not a true decline in AMR burden. By 2050, AMR-attributable deaths in children aged younger than 5 years are projected to decrease by 42·6% with improved paediatric care, while deaths in people aged 70 years and older are expected to increase by more than six times due to ageing, immunosenescence, and higher susceptibility to resistant infections.

Discussion

To our knowledge, this is the first comprehensive estimation of attributable and associated AMR mortality in the EMR (1990–2021) across priority pathogens and pathogen–drug combinations, with projections to 2050. In 2021, the EMR accounted for 8·1% of the global AMR burden (from 1·14 million attributable and 4·71 million associated deaths),[4] mirroring the region's proportional contribution in 1990. Specifically, replacing resistant infections with susceptible ones could have prevented almost 100 000 deaths, and replacing resistant infections with no infection could have prevented almost 400 000 deaths. The burden has shifted towards older age groups, underscoring the growing impact of AMR on ageing populations.

In this study, AMR burden in the EMR decreased between 2020 and 2021, which was likely driven by COVID-19 prevention measures (personal protective equipment, hand hygiene, and distancing)[4,17,18] and

possible mortality displacement, where vulnerable individuals died from COVID-19 rather than bacterial infections.[16] The observed decline was temporary, however, with a surge in AMR rates observed with the easing of pandemic-related measures and travel restrictions, with different resistance profiles; for example, in Egypt, there was an increase in the prevalence of carbapenem-resistant *K pneumoniae* and *E coli*, which is also reinforced in previous publications.[19] Our forecasts reflect this rebound, underscoring that targeted, sustained strategies can reduce AMR.

Our forecasts predict a sharp rise in the AMR burden in the EMR by 2050, with an increase in attributable deaths up to 93·4% and associated deaths up to 89·7% from 2022. All-age mortality rates are set to increase, while age-standardised rates might decline slightly, reflecting demographic shifts such as ageing and higher prevalence of comorbidities (such as obesity and diabetes). Mortality in children younger than 5 years is projected to fall, but deaths in people aged 70 years and older will increase substantially. We specifically focused on these two age categories because they represent the most clinically and epidemiologically vulnerable subgroups of the population. These estimates emphasise the need for timely, age-specific and region-specific strategies to address AMR and strengthen health systems.

Our estimates identified several bacterial pathogens as primary drivers of the estimated burden from 1990–2021, most notably *S pneumoniae*, *K pneumoniae*, *E coli*, and *S aureus*. WHO acknowledges these microorganisms as species of international concern (*K pneumoniae* and *E coli* belong to the critical category and *S aureus* to the high category on the WHO Priority Pathogens List),[20,21] with their relevance corroborated globally and in other regions.[4,22–26] *E coli* and *S aureus* are also an inherent part of the Sustainable Development Goal indicator for AMR (3.d.2),[27] which is important due to the size of their contribution to the projected future AMR burden. Additionally, we have demonstrated a high burden of *A baumannii* and *P aeruginosa*, both in the critical category of WHO Priority Pathogens.[21] However, although WHO ranks *S pneumoniae* as medium priority, its substantial burden in this region suggests its status should be evaluated, considering its consistent impact on AMR mortality. Consequently, our findings emphasise diverse pathogen distribution and the need for region-specific and country-specific interventions.

In prevalence studies done in the six member countries of the Gulf Cooperation Council (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates), *E coli* was identified as the most prevalent resistant microorganism, followed by *K pneumoniae*.[28] In 2022, Bindayna and colleagues[29] reported increasing *E coli* resistance to third-generation cephalosporins, warning this drives carbapenem usage and resistance development. For *S aureus*, methicillin-resistant strains remain prevalent in Kuwait (31%), Oman (37%), Qatar (21%), Saudi Arabia (15–55%), and United Arab Emirates (29%).[30] In Kabul, Afghanistan, methicillin-resistant *S aureus* prevalence reached 56·2%, attributed to inappropriate antimicrobial use.[31] These findings are consistent with our study, where Afghanistan was among the countries with the highest age-standardised rates of attributable and associated AMR burden due to methicillin-resistant *S aureus* in 2021.

Our estimates align with recent regional epidemiological data highlighting other notable resistant pathogens delineated in this study. A 2022 EMR assessment using WHO GLASS data (2017–2019) evaluated selected resistant bacterial infections and regional antimicrobial stewardship and infection prevention capacities.[32] In the EMR assessment study, only bloodstream infections were analysed, and the median proportion was the highest for carbapenem-resistant *Acinetobacter* spp (70·3%). Similarly, our analysis shows carbapenem resistance as a major AMR contributor, with notably high rates of carbapenem-resistant *A baumannii* in Morocco and Sudan.

EMR countries range from high-resource states with advanced technology to those without basic resources, such as safe water, electricity, and sanitation.[33] Excessive antimicrobial usage is also common, with self-medication prevalence ranging from 19–82% in systematic reviews.[34,35] Although sales of antimicrobial drugs without prescription is common in the EMR, there has been substantial decrease in this practice in GCC countries over the years with more stringent enforcement of restrictions.[36] One regional study reported high mean antimicrobial usage (56·9% [range 39–78]), mainly third-generation cephalosporins (26·7%) and penicillins (18·1%).[32] These estimates were higher than those reported in similar studies conducted in Europe,[37] and adherence to prescribing quality indicators was poor.[32] By using the Socio-demographic Index, we found higher scores strongly correlated with lower AMR mortality; however, AMR burden depends on the infectious burden envelope, likely linked to Socio-demographic Index, sanitation, and infection prevention practices, which might influence this finding. These insights should guide future exploration of resistance drivers.[38]

National action plans form the foundation of global AMR governance, requiring swift implementation and regular self-reported monitoring.[39] As country-specific tools adapting global policies to local contexts, we included them in our analysis. One study found EMR national action plans have a high level of mean syntactic overlap—eg, the national action plan for Afghanistan is 50% identical to that for India, and 66% of the national action plan for India matches that for Afghanistan.[39] Although this might indicate there is strong agreement in the represented content, actual policy implementation is likely far less aligned. Additionally, some countries demonstrated more important gaps in several specific

areas than others. One example is the national action plan for Afghanistan, which omitted three of the recommended actions from the Infection Prevention and Control domain from the global AMR action plan;[40] similarly, the national action plan for Pakistan omitted three actions under the Optimised use of antimicrobials domain.[40]

The key step is not merely developing a national action plan, but securing government endorsement and sustained implementation, as reflected in the varied AMR mortality by national action plan status. Regional disparities persist, with infection reduction the priority in areas lacking sanitation, health care and antibiotics, and antimicrobial stewardship more relevant in well-resourced settings.[41] The Muscat Ministerial Manifesto endorsed by 17 countries from the Region, during the Third Global High-level Ministerial Conference in Oman in November, 2022, committed to implementing national action plans with adequate financial resources, milestones and national targets, taking into consideration the One Health approach.[6,41] The Fourth Conference held in Jeddah in November, 2024, endorsed the establishment of an AMR One Health learning hub and regional AMR access and logistics hub within Saudi Arabia.[41] We believe addressing AMR requires not only better national action plan financing and implementation, but also stronger global policy via binding international regulations.

Our study had several limitations. In addition to the sparsity of data linking laboratory results to mortality and disability outcomes,[42] there were issues regarding paucity of data on pathogen distribution by infectious syndrome, and the prevalence of resistance for several key pathogen–drug combinations. Countries with a low Socio-demographic Index often have poor surveillance and laboratory capacity, and thus likely underestimated AMR mortality. Data from politically unstable or conflict-affected countries might be variable or unreliable, affecting quality, availability, and comparability despite model-based adjustments. However, since our estimation method is informed by datapoints from all countries, we relied on regional patterns, covariates, and out-of-sample predictive validity assessment when there was missing data for a specific country. Similarly, although the relative risk for each pathogen–drug combination can differ in accordance with infection severity, comorbidities, access to health care, age, and sex, data sparsity prevented such detailed adjustment, necessitating our use of global relative risks.

Analysing AMR trends was challenged in our study by uneven country data, especially before 2000 when monitoring was sparse and regionally limited. Early estimates therefore relied heavily on modelled trends and covariates. In many low-income and middle-income countries, scarce and non-standardised data hinder tracking resistance trends. COVID-19 further disrupted surveillance by reducing microbiological cultures and outpatient visits, potentially skewing results.[43] Additionally, our AMR burden forecasts to 2050 in the region were limited by the quality and availability of historical data, since trends rely on these estimates. The models forecast overall resistance-related deaths, not pathogen-specific trends, which might reduce accuracy if trends differ. They also exclude potential outbreaks of new resistant pathogens, possibly underestimating future burden.[4] Notably, this study did not include race-specific or ethnicity-specific analyses due to the lack of consistently reported data across countries.

Potential bias and misclassification concerns might arise when coalescing and standardising data from various providers (ie, different levels of care provision), or when there is a need to differentiate community-acquired from health-care-associated infections. Although our case-fatality ratio models distinguish community-acquired and hospital-acquired urogenital and lower respiratory infections, empirical community data are scarce for other syndromes. Reliance on hospital data might also misattribute burden. Selection bias in passive microbial surveillance is also a potential concern, especially when cultures for microbiological analysis are not consistently drawn.[4]

Moreover, the large β-lactam, and particularly carbapenem, resistance burden in *S pneumoniae* warrants further discussion. Our approach assigns the attributable burden to carbapenems for isolates resistant to both third-generation cephalosporins and carbapenems, aligning with Gram-negative mechanisms but potentially overestimating carbapenem resistance in *S pneumoniae*, where resistance primarily stems from penicillin-binding protein mutations.[4,44] Additionally, the mortality effect of *S pneumoniae* resistance was modelled using data from other pathogens with resistance to the same antimicrobial class, introducing further assumptions. Future iterations aim to refine these estimates with data specific to unique *S pneumoniae* resistance mechanisms.

Despite these limitations, our analysis represents one of the most comprehensive efforts to assess bacterial AMR burden in the EMR to date, reflecting the widest available range of data and the use of complex models applied and refined for integrating disparate data sources for GBD analysis.

Bacterial AMR is a major public health threat in the EMR, with substantial future impact projected. Age-specific strategies are needed to address susceptibility in older populations (ie, ≥70 years), and substantial country-level differences mean a single regional action plan will not be sufficient. Important surveillance gaps remain, highlighting the need to improve AMR data collection. Priorities include standardising methods (eg, international protocols), linking microbiology data with clinical outcomes, ensuring routine reporting from all sectors, strengthening labs and workforce, but also expanding digital tools such as electronic health records and laboratory information management systems.

Additionally, educational and awareness campaigns are needed to curb inappropriate antibiotic use, alongside

antimicrobial stewardship programmes in hospitals, outpatient settings, and community pharmacies. Burden studies similar to our study should continue, expanding to more pathogens and indirect AMR effects, as effective policy relies on a full understanding of the problem. The drivers of AMR are interlinked, and thus interlinked solutions are needed.

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Please see appendix 4 (pp 7–9) for more detailed information about individual author contributions to the research, divided into the following categories: managing the overall research enterprise; writing the first draft of the manuscript; primary responsibility for applying analytical methods to produce estimates; primary responsibility for seeking, cataloguing, extracting, or cleaning data; designing or coding figures and tables; providing data or critical feedback on data sources; developing methods or computational machinery; providing critical feedback on methods or results; drafting the manuscript or revising it critically for important intellectual content; and managing the estimation or publications process. The corresponding author and first author had full access to and verified the data and had final responsibility for the decision to submit for publication. The corresponding author confirms all authors approved the final text.

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competing interests. The opinions expressed in this article are those of the authors and do not reflect the official position of WHO. WHO takes no responsibility for the information provided or the views expressed in this article. The boundaries and names shown and the designations used in the maps do not imply the expression of any opinion whatsoever on the part of the WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

Data sharing

The data used in these analyses are available online at the Global Health Data Exchange (https://ghdx.healthdata.org/record/ihme-data/who-region-eastern-mediterranean-amr-1990-2050).

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